CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:NDA 20689

CHEMISTRY REVIEW(S)

DF

JUL 6 1999

CHEMIST'S REVIEW	1. ORGANIZATION HFD-110	2. NDA Number 20-689
3. Name and Address of Applicant (City & State) Hoffmann-La Roche Inc. 340 Kingsland Street Nutley, NJ 07110-1199		4. Supplement(s) Number(s) Date(s)
5. Drug Name Posicor	6. Nonproprietary Name Mibefradil Dihydrochloride	8. Amendments & Other (reports, etc) - Dates Y-002 6/19/99
7. Supplement Provides For:		
9. Pharmacological Category Hypertension and Angina	10. How Dispensed ☒ Rx ☐ OTC	11. Related IND(s)/ NDA(s)/DMF(s)
12. Dosage Form(s) Tablets	13. Potency(ies) 50 and 100 mg	
14. Chemical Name and Structure (1S,2S)-2-[2[[(3-2-Benzimidazoyl)propyl]methylamino] ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-isopropyl-2-naphthylmethoxyacetate dihydrochloride		15. Records/Reports Current ☐ Yes ☐ No Reviewed ☐ Yes ☐ No

16. Comments:

Annual report for the period 4/98 - 4/99.
SUMMARY OF SIGNIFICANT NEW INFORMATION: Roche announced the voluntary withdrawal of POSICOR from the U.S. market on June 8, 1998. This decision was based on evolving information concerning the potential for drug interactions, which may result when POSICOR is taken with certain other medications. POSICOR was also voluntary withdrawn from all markets outside the U.S. Roche distributed "Dear Doctor" letters to physicians nationwide on June 8, 1998 and June 12, 1998.
DISTRIBUTION DATA:
LABELING: No labels submitted (withdrawn). Insert - 25993568-1297 25829852-1297 Revised: December 1997 - satisfactory for DESCRIPTION and HOW SUPPLIED sections.
CHEMISTRY, MANUFACTURING AND CONTROLS CHANGES: Withdrawn. Stability data - none.
NONCLINICAL LABORATORY STUDIES: Studies are reported to IND and IND / / Bibliography of published literature is included in the Appendix.

17. Conclusions and Recommendations:

NAI.

18. REVIEWER		
Name Danute G. Cunningham	Signature /S/	Date Completed July 1, 1999

Distribution: ☐ Original Jacket ☐ Reviewer ☒ Division File ☐ CSO

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16. Comments:

Annual report for the period 6/97 through 4/98.
SUMMARY OF SIGNIFICANT NEW INFORMATION: Meeting were held on 4/3 and 5/1/98 with HFD-110 to discuss the adverse event profile and cases of torsade de poites being spontaneously reported for patients receiving Posicor and the potential for drug-drug interactions. At the May 1 meeting, Roche presented the proposed drug interaction education program to be directed at physicians, pharmacists and patients. In addition, FDA agreed to wait until mid-May for the MACH I study results in evaluating the benefit/risk of POSICOR. On May 27, the results of the MACH I study were reviewed with FDA. On June 8, 1998, Roche Laboratories voluntarily withdrew POSICOR from the U.S. market. The decision was based on evolving information concerning the potential for drug interaction when POSICOR is taken with certain other medications.
DISTRIBUTION DATA:

17. Conclusions and Recommendations:

NAI. Expiration date - 24 months.

18. REVIEWER		
Name Danute G. Cunningham	Signature /S/	Date Completed August 7, 1998

Distribution: ☐ Original Jacket ☐ Reviewer ☒ Division File ☐ CSO

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8-17-98